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Salmeterol Inhalation Powder

DEFINITION

Salmeterol Inhalation Powder for use in dry powder inhalers contains an amount of salmeterol xinafoate ($C_{25}H_{37}NO_4 \cdot C_{11}H_8O_3$) equivalent to NLT 90% and NMT 110% of the labeled amount of salmeterol ($C_{25}H_{37}NO_4$).

IDENTIFICATION

Change to read:

- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the ▲Assay.▲

(IRA 1-Sep-2022)

ASSAY

PROCEDURE

Buffer: 0.15 M [ammonium acetate](#)

Mobile phase: [Methanol](#), *Buffer*, and [formic acid](#) (65:35:0.5)

Diluent: [Methanol](#) and [water](#) (70:30)

System suitability solution: 11 µg/mL of [USP Salmeterol Resolution Check RS](#) in *Diluent*

Standard solution: 9 µg/mL of [USP Salmeterol Xinafoate RS](#) in *Diluent*

Sample solution: Nominally 6 µg/mL of salmeterol free base from NLT 12 unit doses in *Diluent*

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 276 nm

Column: 4.6-mm × 20-cm; 5-µm packing [L1](#)

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 200 µL

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for salmeterol and salmeterol-deoxy are 1.0 and 1.4, respectively.]

Suitability requirements

Resolution: NLT 2.0 between salmeterol and salmeterol-deoxy

Tailing factor: NMT 1.5 for the salmeterol peak

Relative standard deviation: NMT 2% for the salmeterol peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of salmeterol ($C_{25}H_{37}NO_4$) in the portion of the sample taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Salmeterol Xinafoate RS](#) in the *Standard solution* (µg/mL)

C_U = nominal concentration of salmeterol free base in the *Sample solution* (µg/mL), based on the target emitted dose of 47 µg

M_{r1} = molecular weight of salmeterol free base, 415.57

M_{r2} = molecular weight of salmeterol xinafoate, 603.75

Acceptance criteria: 90%–110%

Delete the following:

▲PERFORMANCE TESTS▲ (IRA 1-Sep-2022)

IMPURITIES

Change to read:

• ORGANIC IMPURITIES

[NOTE—Protect the *Sample solution* and *Standard solution* from light.]

Diluent: [Methanol](#) and [water](#) (70:30)

Solution A: [Trifluoroacetic acid](#) in [water](#) (0.05%, v/v)

Solution B: [Trifluoroacetic acid](#) in [acetonitrile](#) (0.05%, v/v)

Mobile phase: See [▲Table 1](#).

Table 1▲ (IRA 1-Sep-2022)

Time	Solution A (%)	Solution B (%)
0	60	40
5	60	40
40	15	85
40.1	60	40
45 ^a	60	40

^a This time may be increased to ensure equilibration.

System suitability solution: 0.1 mg/mL of [USP Salmeterol System Suitability RS](#) in *Diluent*

Standard solution: 2.5 µg/mL of [USP Salmeterol Related Compound H RS](#) in *Diluent*

Sample solution: Nominally 50 µg/mL of salmeterol free base from NLT 10 unit doses prepared as follows. Weigh, and transfer the contents of the appropriate number of unit doses to a suitable volumetric flask. Add 80% of the flask volume of *Diluent*, and sonicate for 5 min. Cool to room temperature, and dilute with *Diluent* to volume. Allow the undissolved material to settle, and inject the supernatant.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 25-cm; 5-µm packing [L1](#)

Column temperature: 30°

Flow rate: 1.0 mL/min

Injection volume: 50 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times are given in [▲Table 2](#).▲ (IRA 1-Sep-2022)]

Suitability requirements

Resolution: NLT 2 between salmeterol-*N*-alkyl and salmeterol related compound H, *System suitability solution*

Relative standard deviation: NMT 2[▲]%▲ (IRA 1-Sep-2022) for salmeterol related compound H, *Standard solution*

Analysis

Samples: ▲*Standard solution* and ▲ (IRA 1-Sep-2022) *Sample solution*